

## SEQUENCE LISTING

<110> DELANSORNE, Rémi  
<110> BONNET, Paule  
<110> PARIS, Jacques

<120> Pharmaceutical compositions based on alpha-cyclodextrin  
for the oral administration of LH-RH analogues

<130> H20058-5US

<150> PCT/EP99/07389  
<151> 1999-09-23

<150> EP98402403.4  
<151> 1998-09-30

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<170> PatentIn Ver. 2.1

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<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence:LH-RH analogue

<220>  
<221> SITE  
<222> (1)  
<223> Xaa is pGlu, D-pGlu, Sar, AcSar, Pro, Ser, D-Ser, Ac-D-Ser,  
Thr, D-Thr, Ac-D-Thr or an optionally substituted and/or acylated  
aromatic D-amino acid

<220>  
<221> SITE  
<222> (2)  
<223> Xaa His or an optionally substituted aromatic D-amino acid

<220>  
<221> SITE  
<222> (3)  
<223> Xaa is an optionally substituted aromatic L- or D-amino acid

<220>  
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<223> Xaa is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr

<220>  
<221> SITE  
<222> (5)  
<223> Xaa is an optionally substituted aromatic L-amino acid  
or an optionally substituted basic L- or D-amino acid

<220>  
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<222> (6)  
<223> Xaa is Gly, (S)-spiolactam-Pro, D-Pro, D-Ser, D-Thr,

D-Cys, D-Met, D-Asn, D-Pen, D-(S-Me)Pen, D-(S-Et)Pen, D-Ser(OBut), D-Asp(OBut), D-Glu(OBut), D-Thr(OBut), D-Cys(OBut), D-Ser(OR1) where R1 is a sugar moiety, an aza-amino acid, D-His which may be substituted on the imidazole ring by a (C1-C6)alkyl, a (C2-C7)acyl or a benzyl group, an aliphatic D-amino acid with a (C1-C8)-alkyl or a (C3-C6)cycloalkyl side chain, an optionally substituted aromatic D-amino acid, D-cyclohexadienyl-Gly, D-perhydronaphthyl-Ala, D-perhydrodiphenyl-Ala or an optionally substituted basic L- or D-amino acid

<220>

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<222> (7)

<223> Xaa is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C1-C4)alkyl group optionally substituted by one or several fluorine atoms

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<221> SITE

<222> (8)

<223> Xaa is an optionally substituted basic L- or D-amino acid

<220>

<221> SITE

<222> (10)

<223> Xaa is GlyNH2, D-AlaNH2, azaGlyNH2 or a group -NHR2 where R2 is a (C1-C4)alkyl which may be substituted by an hydroxy or one or several fluorine atoms, a (C3-C6)cycloalkyl or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl

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1 5 10

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<223> Description of Artificial Sequence:LH-RH analogue

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<223> Xaa is pGlu, Sar or AcSar

<220>

<221> SITE

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<223> Xaa is an optionally substituted aromatic L-amino acid

<220>

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<223> Xaa is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr

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 <223> Xaa is an optionally substituted aromatic L-amino acid

<220>  
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 <222> (6)  
 <223> Xaa is Gly, (S)-spirolactam-Pro, D-Pro, D-Ser, D-Thr, D-Cys, D-Met, D-Pen, D-(S-Me)Pen, D-(S-Et)Pen, D-Ser(OBut), D-Asp(OBut), D-Glu(OBut), D-Thr(OBut), D-Cys(OBut), D-Ser(OR1) where R1 is a sugar moiety, an aza-amino acid, D-His which may be substituted on the imidazole ring by a (C1-C6)alkyl or a benzyl group, an aliphatic D-amino acid with a (C1-C8)alkyl or a (C3-C6)cycloalkyl side chain, an optionally substituted aromatic D-amino acid, D-cyclohexadienyl-Gly, D-perhydronaphthyl-Ala, D-perhydrodiphenyl-Ala or an optionally substituted basic D-amino acid

<220>  
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 <223> Xaa is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C1-C4)alkyl group optionally substituted by one or several fluorine atoms

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 <223> Xaa is an optionally substituted basic L-amino acid

<220>  
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 <223> Xaa is GlyNH<sub>2</sub>, azaGlyNH<sub>2</sub> or a group -NHR<sub>2</sub> where R<sub>2</sub> is a (C1-C4)alkyl which may be substituted by an hydroxy or one or several fluorine atoms, a (C3-C6)cycloalkyl or a heterocyclic radical selected from morpholinyl, pyrrolidinyl and piperidyl

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<220>  
 <223> Description of Artificial Sequence:LH-RH analogue

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 <223> Xaa is pGlu

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<223> Xaa is as defined for SEQ ID NO:2

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<223> Xaa is as defined for SED ID NO:2

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<223> Xaa is as defined for SED ID NO:2

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<222> (7)

<223> Xaa is Leu, Tle, Nle, Hol, Npg, Cha or Ada, which may be N-alpha-substituted by a methyl or ethyl group optionally substituted by one or several fluorine atoms

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5

10

<210> 4

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<213> Artificial Sequence

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<223> Description of Artificial Sequence:LH-RH analogue

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<222> (1)

<223> Xaa is pGlu

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<221> SITE

<222> (3)

<223> Xaa is Phe, Tyr, Trp, 2MeTrp, HPhe, HTyr, Nal, lNal, Bal, Pal, 4Pal or pClPhe

<220>

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<222> (5)

<223> Xaa is Phe, Tyr, Trp, 2MeTrp, HPhe, HTyr, Nal, lNal, Bal, Pal, 4Pal or pClPhe

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<223> Xaa is (S)-spiro lactam-Pro, Gly, D-Pro, D-Ser(OBut), D-Asp(OBut), D-Glu(OBut), D-Thr(OBut), D-Cys(OBut), D-His, D-His(Bzl), D-Ala, D-Leu, D-Tle, D-Nle, D-Hol, D-Npg, D-Cha, D-Phe, D-HPhe, D-Tyr, D-HTyr, D-Trp, D-2MeTrp, D-Nal, D-lNal, D-Bal, D-Pal, D-4Pal, D-pClPhe

D-cyclohexadienyl-Gly, D-perhydronaphtyl-Ala,  
D-perhydrodiphenyl-Ala or D-APhe optionally substituted  
by an aminotriazolyl group

<220>

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<223> Xaa is Leu, Npg or Cha, which may be N-alpha-substituted  
by a methyl group

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<223> Xaa is GlyNH<sub>2</sub>, azaGlyNH<sub>2</sub> or -NC<sub>2</sub>H<sub>5</sub>

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Xaa	His	Xaa	Ser	Xaa	Xaa	Xaa	Arg	Pro	Xaa
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<210> 5

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:LH-RH analogue

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<221> SITE

<222> (1)

<223> Xaa is pGlu

<220>

<221> SITE

<222> (6)

<223> Xaa is (S)-spirolactam-Pro, D-Leu, D-Ala, D-Nal,  
D-Phe, D-Ser(OBut) or D-Trp

<220>

<221> SITE

<222> (7)

<223> Xaa is Leu, MeLeu, Npg or MeNpg

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<223> Xaa is GlyNH<sub>2</sub>, azaGlyNH<sub>2</sub> or -NC<sub>2</sub>H<sub>5</sub>

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Xaa	His	Trp	Ser	Tyr	Xaa	Xaa	Arg	Pro	Xaa
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<213> Artificial Sequence

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<223> Description of Artificial Sequence:LH-RH analogue

<220>  
<221> SITE  
<222> (1)  
<223> Xaa is pGlu, D-pGlu, Sar, AcSar, Pro thereof, Ser, D-Ser, Ac-D-Ser, Thr, D-Thr, Ac-D-Thr or an optionally substituted and/or acylated aromatic D-amino acid

<220>  
<221> SITE  
<222> (2)  
<223> Xaa is an optionally substituted aromatic D-amino acid

<220>  
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<222> (3)  
<223> Xaa is an optionally substituted aromatic L- or D-amino acid

<220>  
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<223> Xaa is Ala, Ser, D-Ser, MeSer, Ser(OBut), Ser(OBzl) or Thr

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<223> Xaa is an optionally substituted aromatic L-amino acid or an optionally substituted basic L- or D-amino acid

<220>  
<221> SITE  
<222> (6)  
<223> Xaa is Gly, (S)-spirolactam-Pro, D-Pro, D-Ser, D-Thr, D-Cys, D-Met, D-Asn, D-Pen, D-(S-Me)Pen, D-(S-Et)Pen, D-Ser(OBut), D-Asp(OBut), D-Glu(O-But), D-Thr(O-But), D-Cys(O-But), D-Ser(O-R1) where R1 is a sugar moiety, an aliphatic D-amino acid with a (C1-C8)alkyl or a (C3-C6)cycloalkyl side chain, an optionally substituted aromatic D-amino acid, D-cyclohexadienyl-Gly, D-perhydronaphthyl-Ala, D-perhydrodiphenyl-Ala or an optionally substituted basic L- or D-amino acid

<220>  
<221> SITE  
<222> (7)  
<223> Xaa is a linear, branched or cyclic aliphatic L-amino acid of 3 to 20 carbon atoms which may be N-alpha-substituted by a (C1-C4)alkyl group optionally substituted by one or several fluorine atoms

<220>  
<221> SITE  
<222> (8)  
<223> Xaa is an optionally substituted basic L- or D-amino acid

<220>  
<221> SITE  
<222> (10)  
<223> Xaa is GlyNH2 or D-AlaNH2

<400> 6

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Pro Xaa  
1 5 10

<210> 7

<211> 10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence:LH-RH analogue

<220>

<221> SITE

<222> (1)

<223> Xaa is Ac-D-Nal

<220>

<221> SITE

<222> (2)

<223> Xaa is D-pClPhe

<220>

<221> SITE

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<223> Xaa is D-Pal

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<221> SITE

<222> (5)

<223> Xaa is Tyr, HTyr, MeTyr, MeHTyr, NicLys or IprLys

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<223> Xaa is (S)-spiro lactam-Pro, D-Arg, D-NicLys, D-IprLys,  
D-Cit, D-HCit or D-Asn

<220>

<221> SITE

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<221> SITE

<222> (8)

<223> Xaa is Arg, NicLys or IprLys

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<221> SITE

<222> (10)

<223> Xaa is DAlaNH<sub>2</sub>

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